REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested. Claims 42-70 are pending. Claims 32-35 have been cancelled without prejudice following withdrawal from consideration by the examiner and claims 71-72 have been cancelled. Applicants expressly reserves the right to pursue such claims in continuation and/or divisional applications.

Applicants wish to point out that the present invention is based on the surprising discovery that molecules with structural characteristics of a J chain and derivatives thereof, are capable of specifically binding to a factor preferentially distributed on an epithelial surface and, in some cases, causing internalization. The claims are generally directed to a composition for delivery of a biological agent to a basolateral factor of an epithelial surface, the composition comprising a targeting molecule linked to at least one biological agent. Common to the claims is the requirement that the targeting molecule comprise a J chain or portion thereof and the CH2 and CH3 domains of an IgA or IgM. Also required is that the targeting molecule not comprise a full-length immunoglobulin, and that the biological agent not be native to the targeting molecule and not be iodine.

The amendments find ample basis in the specification and claims as originally filed. For example, support for "CH2 and CH3 domains of an IgA or IgM" is found Page 9, lines 11-16; page 14, lines 25-28; and Table 1 p. 28-29. Accordingly, the amendments raise no issue of new matter.

CLAIM OBJECTIONS

Claim 56 is objected to as being of improper dependent form for allegedly failing to further limit the claim from which it depends. It is alleged that a J chain is a polypeptide and all polypeptides have a C-terminal domain. Applicants have amended claim 56 to more clearly specify the feature that is further limiting. Accordingly, the objection has been obviated.

Claims 71 and 72 are objected to as being of improper dependent form for allegedly failing to further limit the claim from which it depends. Applicants have cancelled claims 71 and 72, thus obviating the objection.

REJECTION UNDER OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 42-72 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-23, 25-37 of U.S. Patent No. 6,045,774. A suitable terminal disclaimer has been filed herewith.

Claims 42-72 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 22-28, 31, and 65-97 of U.S. Serial no. 08/782,481. Applicant respectfully requests that the examiner defer this issue until the time that allowable subject matter has been identified in either application.

Claims 42-72 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-3 of U.S. Patent no. 6,251,392. A suitable terminal disclaimer has been filed herewith.

Claims 42-72 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-36 of U.S. Patent no. 6,391,280. A suitable terminal disclaimer has been filed herewith.

Claims 42-72 have been **provisionally** rejected under the judicially created doctrine of obviousness type double patenting over claims of U.S. serial no. 10/062,467. As prosecution in both applications is ongoing, Applicant respectfully requests that the examiner defer this issue until the time that allowable subject matter has been identified in either application.

REJECTION UNDER 35 USC § 112 FIRST PARAGRAPH

Claims 42-72 have been rejected under the 35 USC § 112, first paragraph, written description and enablement requirements because a J chain or portion thereof allegedly does not target the polyimmunoglobulin receptor in the absence of the hinge region of the

Fc. Although Applicant respectfully disagrees with this position, for the purposes of furthering prosecution in this case, the claims have been amended to require the targeting agent include the CH2 and CH3 domains of an IgA or IgM. Accordingly, the rejections for alleged lack of written description and enablement have been obviated.

REJECTION UNDER 35 USC § 112 SECOND PARAGRAPH

Claims 48, 53 and 55 have been rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for the phrase "comprises amino acid sequence from." Although Applicant does not agree with the rejection, nevertheless, the claims have been amended to obviate this issue.

Claims 58 and 60 have been rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for the phrase "comprises an amino acid sequence from." The rejection has been obviated by amendment of claims 58 and 60.

Claims 42-72 have been rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for the phrase "specifically binds." It is alleged that the specification does not identify that material element or combination of elements which is unique to and, therefore, definitive of "specifically binds." It is further alleged that an artisan cannot determine what additional for material functional limitations are placed upon a claim by the presence of this element. The rejection is respectively traversed.

35 U.S.C. § 112, second paragraph, requires only reasonable precision in delineating the bounds of the claimed invention. The claim language is satisfactory if it reasonably "apprise[s] those skilled in the art . . . [of the bound of the claimed invention] and is as precise as the subject matter permits." Shatterproof Glass Corp. v. Libby-Owens ford Co., 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed Cir. 1985).

First, it is respectfully submitted that the instant rejection is deficient because it does not explain why the phrase "specifically binds" is allegedly indefinite. The rejection is wholly unsupported and provides nothing for Applicant to rebut.

Second, one skilled in the art would readily acknowledge that the term "specifically binds" is clear and in fact very well known. In addition, the specification provides a

definition of this term at page 8, consistent with its well known art meaning. In view of the above, it is respectively submitted that the skilled artisan also would readily acknowledge that there is nothing unclear about the term "specifically binds."

Applicant has deleted the term specifically binds from the claims because it is a well known property of J chain comprising molecules. Nevertheless, Applicant respectfully requests that the examiner acknowledge the noted deficiencies associated with the rejection in the next communication.

REJECTION UNDER 35 U.S.C. § 103(a)

Rejection over Max in view of Janknecht

The rejection of claims 42, 43, 45, 51, 52, 54-57, 59, 67, 68 and 70-72 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Max (AP cited by Applicants) and Janknecht (uu32 cited by Applicants) is respectfully traversed. Applicants submit that the Examiner has not established a motivation to combine the publications as suggested by the Examiner. Moreover, even if combined as suggested, the publications do not teach or suggest each and every element of the present claims. Thus, no *prima facie* case of obviousness has been established.

To establish a *prima facie* case of obviousness, three criteria must be met; there must be some motivation or suggestion, either in the cited publications or in knowledge available to one skilled in the art, to modify or combine the cited publications; there must be a reasonable expectation of success in combining the publications to achieve the claimed invention; and the publications must teach or suggest all of the claim limitations. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2142. In analyzing obviousness, the Court of Appeals for the Federal Circuit has repeatedly cautioned that:

> [t]he factual inquiry... must be based upon objective evidence of record.... [T]he best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references.... [P]articular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.

In re Sang-Su Lee, 277 F.3d 1338, 1343 (internal citations omitted).

In the present case, the instant claims cover a composition for delivery of a biological agent to a basolateral factor of an epithelial surface. The composition comprises a targeting molecule linked to at least one biological agent, wherein the targeting molecule comprises a J chain or portion thereof and the CH2 and CH3 domains of IgA or IgM and wherein the targeting molecule is not a full-length immunoglobulin. Further required is that the biological agent not be native to the targeting molecule and the biological agent not be iodine.

Max discloses the nucleotide sequence encoding a J chain from a genomic clone. Max does not teach to link to J chain or any targeting agent. Max does not disclose a targeting molecule linked to at least one biological agent, wherein the targeting molecule comprises a J chain or portion thereof and the CH2 and CH3 domains of IgA or IgM and wherein the targeting molecule is not a full-length immunoglobulin. Max also does not disclose that the biological agent not be native to the targeting molecule and the biological agent not be iodine. In fact, Max does not teach or suggest any type of targeting molecule for delivery of a biological agent.

Janknecht discloses the production of eukaryotic proteins from vectors where the proteins are expressed to include a C-terminal or N-terminal polyhistidine sequence. The histidine tag is used to allow rapid enrichment of these proteins by metal chelate affinity chromatography. Janknecht, like that of Max, does not disclose a targeting molecule linked to at least one biological agent, wherein the targeting molecule comprises a J chain or portion thereof and the CH2 and CH3 domains of IgA or IgM and wherein the targeting molecule is not a full-length immunoglobulin.

The examiner has failed to meet his/her burden of citing to specific evidence that Janknecht teach a biological agent. Nothing has been cited which demonstrates that a polyhistidine sequence is derived from a cell. Although it is not Applicant's burden to prove otherwise, it is pointed out that if such sequences were resident in cells, there would be no advantage to using metal chelate affinity chromatography for recombinant protein purification. Furthermore, the examiner's position that polyhistidine is derived

from a cell because histidine comes from a cell is based on an absurd reading which would be rejected by one of ordinary skill in the art.

Also, nothing has been cited which demonstrates that a polyhistidine sequence is a biological agent because it modifies a property of a cell. The examiner's position that the presence or absence of the alleged biological agent itself constitutes a cell property (Office action, page 13, lines 3-8) is an absurd reading based on improper circular logic, which would be rejected by one of ordinary skill. The only reasonable reading of this requirement is that the property of cell that is modified must be a property that exists in the absence of the alleged biological agent. A prima facie rejection requires that the examiner identify which pre-existing property of the cell is modified by the polyhistidine sequence. The office action fails to identify any such preexisting property.

The rejection is also defective because it fails to provide a specific basis for motivation to combine. Although there may be interest in using polyhistidine for purifying certain recombinant proteins, the examiner has cited to no teaching that applies this interest to immunoglobulins. A J chain containing targeting agent that includes the CH2 and CH3 domains of IgA or IgM is a protein with unique characteristics that lends itself to ready isolation without resort to a polyhistidine tag.

In addition to the fact that the combination of art fails to teach all elements of the invention, Applicants respectfully submit that, when the cited publications are properly considered, it is apparent that any motivation to modify or combine the cited publications in order to provide the instant claims can only be gleaned in hindsight using the instant specification as a guide. Thus, in the absence of the teachings of the instant application, the skilled artisan would not have a motivation to combine the publications as the Examiner contends. Because a motivation to modify the cited art must be found in the prior art, and not in applicant's own disclosure, no *prima facie* case of obviousness has been established. *See, e.g., In re Vaeck,* 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2142.

Accordingly, as the claims are not obvious over Max in view of Janknecht, reconsideration and withdrawal of the rejection is respectively requested.

Rejection over Max in view of Marston and Baxter

The rejection of claims 42, 43, 45, 51, 52, 54-57, 59, 62, 67, 68 and 70-72 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Max (AP cited by Applicants) and Marston (z32) and Baxter (a32) is respectfully traversed. Applicants submit that the Examiner has not established a motivation to combine the publications as suggested by the Examiner. Moreover, even if combined as suggested, the publications do not teach or suggest each and every element of the present claims. Thus, no *prima facie* case of obviousness has been established.

The many deficiencies in the teachings of Max who does not teach any targeting molecule have been discussed above. Marston allegedly teaches to express proteins in bacteria as a fusion to a bacterial protein such as beta galactosidase, while Baxter allegedly teaches to express beta endorphin as a fusion to beta galactosidase. The rejection is deficient because none of the references alone or combined teach a targeting molecule linked to at least one biological agent, wherein the targeting molecule comprises a J chain or portion thereof and the CH2 and CH3 domains of IgA or IgM and wherein the targeting molecule is not a full-length immunoglobulin.

The rejection is also defective because it fails to provide a specific basis for motivation to combine. Although as the examiner notes that Marston states that the supply of many eukaryotic proteins of clinical or industrial use is often limited by their low natural availability, J chain containing immunoglobulins art relatively abundant proteins.

In addition to the fact that the combination of art fails to teach all elements of the invention, Applicants respectfully submit that, when the cited publications are properly considered, it is apparent that any motivation to modify or combine the cited publications in order to provide the instant claims can only be gleaned in hindsight using the instant specification as a guide. Thus, in the absence of the teachings of the instant application, the skilled artisan would not have a motivation to combine the publications as the Examiner contends. Because a motivation to modify the cited art must be found in the prior art, and not in applicant's own disclosure, no *prima facie* case of obviousness has

been established. *See, e.g., In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2142.

Accordingly, as the claims are not obvious over the combination of Max, Marston and Baxter, reconsideration and withdrawal of the rejection is respectively requested.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is urged to contact the undersigned by telephone to address any outstanding issues standing in the way of an allowance.

Respectfully submitted,

Date: July 24, 2003

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